

WHAT IS CLAIMED IS:

1. A method of increasing the ability of an adenovirus to transduce a specific cell type, comprising the step of:

modifying a gene encoding an adenoviral capsid protein,

5 wherein said modification increases the ability of said adenovirus to transduce a specific cell type.

2. The method of claim 1, wherein said gene encoding said capsid protein is modified by introducing a single chain antibody
10 into said gene.

3. The method of claim 2, wherein said single chain antibody is directed towards a protein, wherein said protein is specific to a cell type.

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4. The method of claim 3, wherein said cell type is a tumor cell.

5. The method of claim 3, wherein said protein is a cell-
20 surface protein.

6. The method of claim 1, wherein said capsid gene is a minor capsid gene.

7. The method of claim 6, wherein said minor capsid gene
5 is selected from the group consisting of pIIIa and pIX.

8. The method of claim 1, wherein said modified capsid protein retains its native display profile.

10 9. The method of claim 1, wherein said adenovirus exhibits CAR-independent gene transfer.

10. The method of claim 1, wherein said adenovirus further comprises an additional modification to an adenovirus fiber knob,
15 wherein said modification to said fiber knob ablates the native tropism of said adenovirus.

11. The method of claim 1, wherein the adenoviral vector encoding said adenovirus further comprises a therapeutic gene.

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12. A method of killing tumor cells in an individual, comprising the steps of:

administering to said individual an effective amount of recombinant adenoviruses comprising a therapeutic gene that
5 converts a non-toxic compound to a toxic compound and a gene encoding an adenoviral capsid protein modified by introducing a single chain antibody into said protein; and
treating said individual with said non-toxic compound.

10 13. The method of claim 12, wherein said therapeutic gene is herpes simplex virus-thymidine kinase gene and said non-toxic compound is ganciclovir.

14. The method of claim 12, wherein said single chain
15 antibody is directed towards a protein specific to a cell type.

15. The method of claim 14, wherein said cell type is a tumor cell.

20 16. The method of claim 14, wherein said protein is a cell-surface protein.

17. The method of claim 12, wherein said capsid protein is a minor capsid protein.

5 18. The method of claim 17, wherein said minor capsid protein is selected from the group consisting of pIIIa and pIX.

19. The method of claim 12, wherein said modified capsid protein retains its native display profile.

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20. The method of claim 12, wherein said adenovirus exhibits CAR-independent gene transfer.

21. The method of claim 12, wherein said adenovirus further
15 comprises an additional modification to an adenovirus fiber knob, wherein said modification to said fiber knob ablates the native tropism of said adenovirus.

22. A method of monitoring the replication and distribution
20 of adenoviral vectors in a subject, said method comprises the steps of:

constructing an adenoviral vector that expresses a fusion protein comprising an adenoviral structural protein and a fluorescent tag;

administering said adenoviral vector to said subject; and

5 detecting fluorescence of said vector in said subject, wherein the level of said fluorescence correlates with the level of viral replication and localization of said vector in said subject.

23. The method of claim 22, wherein said subject is an
10 animal or a human.

24. The method of claim 22, wherein said adenoviral structural protein is selected from the group consisting of capsid protein pIX, core protein mu, core protein V and core protein VII.
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25. The method of claim 22, wherein said fluorescent tag is selected from the group consisting of enhanced green fluorescent protein, green fluorescent protein, *Discosoma* red fluorescent protein, far-red fluorescent protein, monomeric red fluorescent
20 protein and *Renilla* luciferase.

26. The method of claim 22, wherein said detection of fluorescence involves a method selected from the group consisting of whole body fluorescence imaging, bronchoscopy, endoscopy and laparoscopy.

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27. The method of claim 22, wherein said adenoviral vector further carries a therapeutic gene.